

Further, the manner of treating or preventing these disorders by the administration of appropriate levels of folic acid to women taking oral contraceptives is also specifically set forth in this section of the specification and is supported by numerous citations to the art. Additional teachings regarding current recommendations in the art for daily folic acid doses, and indication-specific dosages based on these recommendations, are found at page 16, line 27 to page 17, line 7. In view of the specific teachings provided in the specification and the references cited therein, as well as the general level of knowledge in the art regarding the treatment or prevention of cervical displasia and cervical carcinoma resulting from insufficient folic acid levels, applicants maintain that the rejection issued under the first paragraph of § 112 is not well-taken and should be withdrawn.

Claim 21 has also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Mortimer in view of Tepic. As discussed below, the combination of Mortimer and Tepic relied on by the Examiner fails to render the claimed invention obvious.

Claim 21 defines a method for administering folic acid which comprises administering to a subject for whom oral contraception is indicated a pharmaceutical composition that combines, in a single dosage, both an oral contraceptive and folic acid. Folic acid is administered in an amount sufficient to treat or prevent cervical displasia or cervical carcinoma in instances where those disorders result from folic acid deficiency and are treatable or preventable by administering sufficient folic acid to prevent such deficiency. Since oral contraceptives are typically administered chronically over regular and extended intervals, the method taught by the invention provides for sustained administration of folic acid at dosage levels sufficient to maintain normal bodily stores and to ensure that sufficient folic acid is available in cases of increased bodily folic acid requirements. Such a method of administering folic acid would not be obvious to a person skilled in the art based on the combined teachings of Mortimer and Tepic.

Mortimer is primarily concerned with a method for treating or preventing hair loss in men. To this end, Mortimer teaches the use of progestin formulations, in particular medroxyprogesterone acetate, together with vitamin and mineral supplements to treat or prevent male pattern baldness. Mortimer notes that progestins cause desquamation of superficial cells of the vaginal mucosa, inhibit ferning of the cervical mucosa and induce withdrawal bleeds in oestrogen primed women. Mortimer also observes that many individuals for whom progestin therapy is appropriate also benefit from treatment with folic acid. According to Mortimer, this is

the case because such individuals often have poor diets due to depression because of their general medical condition and because such patients are often in need of new tissue growth or better fertility.

Mortimer nowhere teaches or even suggests a method of administering folic acid which includes administering to the subject a pharmaceutical preparation that comprises both an oral contraceptive and folic acid. Nor does Mortimer demonstrate any appreciation of the advantages associated with the claimed method, which prevents folic acid deficiency in subjects taking oral contraceptives by providing for the chronic administration of an appropriate amount of folic acid over extended intervals via the administration of a composition that combines folic acid and an oral contraceptive in a single dosage. Mortimer also fails to provide a single example or even any specifics regarding a method of administering folic acid to a subject for whom oral contraception is indicated, much less such a method which includes administering a pharmaceutical composition comprising both an oral contraceptive and folic acid.

As for US Patent No. 5,851,985 to Tepic et al., this reference relates to a method of treating tumors by arginine deprivation. According to Tepic, tumor cells are destroyed by depriving the cells of the essential amino acid arginine, thereby inhibiting protein synthesis. This is accomplished by dialyzing the blood of a patient to remove arginine from the blood for a time sufficient to cause tumor cells to die. According to Tepic, the effectiveness of the treatment is due entirely to the removal of arginine from the blood by means of an extracorporeal exchange between the blood and a dialyzing fluid across a molecular sieve membrane. Tepic supplements the dialyzing fluid with a number of water-soluble vitamins, major inorganic salts, folic acid and biotin. These components of the dialysis fluid are not active in inhibiting protein synthesis in tumor cells but are added to the dialyzing solution to insure that proper blood levels of these components are maintained during and after the dialysis treatment. No fair reading of Tepic provides any suggestion that folic acid is effective in killing cervical carcinoma cells, and Tepic certainly makes no suggestion regarding a method of administering folic acid wherein folic acid is combined in a single dosage with an oral contraceptive. Accordingly, a person skilled in the art would have no motivation to combine the teachings of this reference with Mortimer in the manner suggested by the Examiner.

In view of the foregoing, applicants maintain that amended claim 21 patentably distinguishes over the cited art and is otherwise in condition for allowance. Claims 22 and 23, both depend directly or indirectly from claim 21 and are allowable for at least the same

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reasons discussed above with respect to claim 21. Accordingly, applicants request that a  
Notice of Allowance directed to claims 21-23 be issued at the earliest possible date.

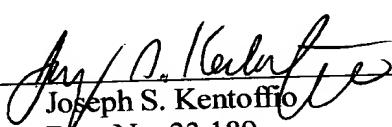
Attached hereto is a marked-up version of the changes made to the claims by the current  
amendment. The attached pages are captioned "Version With Markings To Show Changes  
Made".

An Information Disclosure Statement in accordance with 37 C.F.R. § 1.97 (c) is being  
submitted herewith.

Applicants do not believe any fees are required in connection with the filing of this  
Response; however, should any fees be required please charge Deposit Account No. 10-  
0750/ORT-1316/JSK.

Should the Examiner have any questions regarding this Response, please contact the  
undersigned attorney at the telephone number listed.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CORRECTIONS MADE

In the Claims

Please amend claim 21 as follows:

21. (Amended) A method of administering folic acid to a subject for whom an oral contraceptive is indicated for preventing pregnancy, which comprises administering to the subject, a pharmaceutical composition, wherein

- (c) the pharmaceutical composition comprises an oral contraceptive for preventing pregnancy in a subject, and folic acid in an amount sufficient to treat or prevent cervical dysplasia or cervical carcinoma which (i) afflicts subjects for whom the oral contraceptive is indicated at a higher-than-normal incidence, (ii) results from folic acid deficiency, and (iii) is treatable or preventable by folic acid administration, and
- (d) the subject is from a population whose members are afflicted with, or are predisposed to become afflicted with, cervical dysplasia or cervical carcinoma at a higher than normal incidence, the disorder being treatable or preventable by folic acid administration.

Please add the following new claims:

22. (New) The method of claim 21, wherein the composition comprises from about 25 µg to about 1 g of folic acid.

23. (New) The method of claim 22, wherein the composition comprises about 400 µg of folic acid.